UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,337	07/14/2006	Akira Nishiyama	Q95734	2433

23373 7590 06/24/2009
SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
06/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,337	NISHIYAMA ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6 and 10-15* is/are pending in the application.

4a) Of the above claim(s) *6,11,12 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,13 and 15* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/7/09 has been entered.

Claims 1, 6, and 13 are amended.

Claims 2-5 are cancelled.

Claims 14 and 15 are newly presented.

Claims 1, 6, and 10-15 are presently pending.

Election/Restrictions

Claims 6, 11-12, and 14 remain/are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/16/07.

Claims 1, 10, 13, and 15 are presently considered.

Claim Status—Cancelled Claims

In light of the cancellation of Claims 2-5, all prior rejections and/or objections to such claims are withdrawn.

Claim Objections

Claim 13 objected to because of the following informalities:

Claim 13 recites "producing an aqueous solution of 2-acetyl-butyrolactone [] into 5-hydroxy-2-pentanone". You do not produce a reaction, you perform the reaction. It would be remedial to amend the limitation to recite "reducing an aqueous solution of 2-acetyl-butyrolactone [] into 5-hydroxy-2-pentanone".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of the amendments, the rejections of Claims 1 and 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 13, the phrase "optionally" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites asymmetrical reduction of a compound in the presence of cultured cells, crude extract, lyophilized cells, or acetone-dried cells of a microorganism, or any disrupted product of these cells, wherein the cells have a generic "ability" to produce an enzyme of a Markush group and further have an activity to reduce the compound accordingly, or alternatively the cells have a generic "ability" to produce a reducing enzyme of a second markush group, and have an ability to reduce the compound accordingly. The depending claims also encompass the broader genera.

The claim is clearly reaching through to anything which produces the desired reduction. The enzymes are not even required to be produced, much less present in the curde extract, and may even be disrupted, according to the claim. Moreover, the claim clearly detaches the enzyme from the activity, listing it separately, to the point of appearing to be an intentional detachment from everything. Still further, the crude extract is not required to be of the cells, and only the acetone cells of a separate group of generic microorganisms are even required to have an ability

to produce the enzyme. However, they are not even required to produce the enzyme. Hence, the Claims read on a generic reduction in the presence of the any cultured cell, any crude extract of anything, any lyophilized cells, or any acetone-dried cells of a microorganism capable of producing any of the enzymes. However, for the record, it is a fact that any microorganism can produce these enzymes.

Such total detachment provides a generic embodiment where any activity to produce the reduction is allowed, as long these other one of these other generic compositions are present. Moreover, Applicant has not described anything as far as the generic other component which may so-produce the reduction, when present with the various generic compositions.

Fruther, as is shown throughout the specification, the various enzymes are meant to produce the reduction when they are present.

Hence, the Artisan would not have understood Applicant to have been possession of the invention as presently claimed at the time of filing.

Claim Rejections - 35 USC § 112 - new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, and 15 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The subject claims are drawn to a generic reducing enzyme derived of C. magnoliae IFO0705, C. malis IFO10003 or D. riboflavina IFO13584, Rhodococcus sp. KNK01, and R. glutinus IFO415, which organisms have the ability to affect the claimed reduction.

The specification at best does not provide that these organisms and the breadth of enzymes are encompassed to perform the reduction, but that, from these organisms, the specific sequences of a specific reducing gene was transformed into cells which are deposited (e.g., paragraph 0051 of the publication). Hence, there is no intent in the specification to utilize these organisms, but to utilize the gene expressed product of the various cells that plasmids are transformed into. In fact, no description is given for these cells and what is important, but only that the "reducing enzyme" was placed in specific plasmids and transformed into the various FERM BP deposited cell lines: i.e., FERM BP- 5835, 7117, 08485, 08545, and 7858.

Moreover, as this is new matter, no consideration of the prior is required, as such would be obviousness, and obviousness does not provide for possession.

Further, Applicant has not provided any basis for possession, as is their duty, not the Examiner's duty.

Hence, the Artisan could not have determined Applicant to have been in possession of the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 13 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Whitney, et al. (1974) Advances in Chemistry, Vol. 130: 270-80 and the general knowledge in the art, as now further evidenced by pp. 680-81 and 853-54 of Morrison and Boyd's Organic Chemistry Text, 3rd Edition, by Allyn and Bacon, New York, NY., for reasons of record.

The rejection has been fleshed out, as it appears that Applicant does not understand the rejection

Whitney teaches the reduction of 5-hydroxy-2-pentanone by chelated lithium compounds, to yield optically active 1,4-pentanediol (e.g., p. 277). Moreover, the compounds exhibit stereoselective reduction, otherwise the resultant compound would not be optically active.

However, Whitney does not teach obtaining the compound for reduction from a method comprising acid hydrolysis of 2-hydroxy-gamma-butyrolactone.

On the other hand, it is well known that 2-hydroxy-gamma-butyrolactone has been available for years, and even Applicant's specification states that the availability of such is superior to other sources, evidencing Applicant's acknowledgement of the Art. This is Official Notice.

Specifically, it has been long well known, even to a first year organic chemist, that acid hydrolysis of a ester will yield a carboxyl group and a hydroxyl group on the appropriate carbons

(Morrison and Boyd, pp. 680-81). Hence, such acid hydrolysis will yield 2-keto-3-carboxyl-pentanol. Further acid hydrolysis of the beta keto-carboxylate, will elminate the carboxyl group (Morrison and Boyd, pp. 680-81). Therefore, it was well known and obvious to perform an acid hydrolysis to make 2-acetyl-gamma-butyrolactone into 5-hydroxy-2-pentanone.

Second, it is clear that Whitney teaches asymmetric reduction of 5-hydroxy-2-pentanone can be performed to form optically active 1, 4-pentanediol (Run 13 and p. 276).

Hence, at the time of the invention, the claimed invention would have been obvious. The Artisan would be motivated to perform the acid hydrolysis to perform a reduction and thereby obtain the compound of interest. Moreover, the Artisan would have had a reasonable expectation of success, as the art of organic chemistry was already fleshed out for the methods involved in such syntheses.

Response to Argument – 103 - Whitney and general knowledge

Applicant's argument of 4/7/09 has been fully considered but is not found persuasive.

Applicant argues, citing case law, that an unexpected result does not need to be part of the claim to make the claim patentable, citing case law (p. 9, penultimate paragraph).

Such is not persuasive. In the cited case, In re Wiechart, a specific structural compound was found patentable over an obviousness-type rejection, and the compound, being non-obvious is necessarily non-obvious, and it is due to its structure. Therefore, not claiming the result is not holding in Wiechart. However, and more importantly, Applicant has claimed a method in which each compound is exactly the same in structure and the method steps are the same; and hence, no distinctness can be obtained. Hence, the rejection for obviousness does not require consideration

of unexpected results. The only way such consideration require consideration is if Applicant claims the unexpected result.

Applicant argues that the purity of optically-active 1,4-pentanediol was increased when an acid or neutralized aqueous solution of 5-hydroxy-2-pentanone produced by acid hydrolysis of 2-acetyl-gamma-butyrolactone was utilized in the reduction step. Further, Applicant argues that Whitney does not describe such, and that it would not work for such reductions as Whitney. Hence, Applicant argues, the result is not an unpredicted result (pp. 9-10, paragraph bridging).

Such is not persuasive. Applicant's specification teaches that the purity of 5-hydroxy-2-pentanone can be decreased by dehydration condensation by itself, of which official notice is given that such is well known to a first year college student of Organic Chemistry (paragraph 0026 of the publication). Also taught in the same paragraph is that acid hydrolysis of 2-acetyl-gamma-butyrolactone in the presence of acid will yield the same 5-hydroxy-2-pentanone. Hence, these are just methods of obtaining the same compound: either (i) utilize purchased 5-hydroxy-2-pentanone, and note that its purity can be decreased over time, or (ii) acid-hydrolyze 2-acetyl-gamma-butyrolactone. **Applicant's argued teaching is not a teaching that the obtained product of further reactions is more pure. In fact, it notifies the Artisan of what he is well aware of: purity of an initial product may be lowered over time, and hence, purification of the product from the source obtained, or purchasing a new source of higher purity may be required. It has naught to do with the product obtained by the chemical asymmetric reduction.**

Applicant broadly argues that it is impossible to reduce 5-hydroxy-2-pentanone in an aqueous solution by the method described by Whitney (pp. 9-10, paragraph bridging).

Broad argument by the Attorney does not supplant the requirement to provide specific reasoning and/or evidence to rebut the Examiner's rejection. However, it is noted that there is no requirement in the claims to maintain the composition in acid conditions during the reduction of 5-hydroxy-2-pentanone.

Hence, the rejection is maintained and further clarified by the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10 and 13 remain rejected, and Claim 15 is newly rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes encoded in pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, to produce R, R, R, S, and S enantiomers, respectively, does not reasonably provide enablement for the breadth of products (e.g., any crude extract, any lyophilized cells, any acetone-dried cells of a microorganisms, and any disrupted enzymes) and the breadth of any reducing enzyme from the organisms and the breadth of enantiomers for any particular source, for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is noted that Applicant has attempted to amend Claim 1 to somewhat embrace the enzymes, however, it is also clear that in their attempt to obtain coverage for anything and

everything, they have specifically detached the important aspect of the specific enzymes which are shown in the specification to work (See rejection for new matter, above).

The encompass the production of optically active 1,4-pentanediol from 5-hydroxy-2-pentanone, by any substance, even disrupted, from a cell or from a markush of cells which have an ability to reduce the so—claimed compounds, accordingly.

The nature of the invention is the selective reduction of 5-hydroxy-2-pentanone with any enzyme to produce optically active 1,4-pentane diol. The invention is generally enabled for the use of standard organic chemistry methods, e.g., Whitney, et al. (1974) Advances in Chemistry, Vol. 130: 270-80. The organic chemist is well aware of organic chemistry, and the methods to produce the product are generally within the grasp of the organic chemist without undue experimentation. However, the claims also, importantly, encompass the use of biochemical enzymes (i.e., protein enzymes) to produce the same. This is where the problems in the Art exist.

The closest Prior Art with regard to biochemical reductions are those of Wada, et al. (1999) Journal of Bioscience and Bioengineering, 87(2): 144-48 and Wada, et al. (1998) Bioscience and Biotechnological Biochemistry.

The Wada (1998) article teaches and reviews a general characterization of several enzymes from various organisms, which produce stereoselective reductions of a distinct molecule, which have stereoselectivity which is not commensurate with any specific enantiomer, such that, from this Article, the Artisan could not reasonably predict that any particular enantiomer would be made in any specific organism (DISCUSSION), other than that the specific enzyme will produce the product found.

The Wada (1999) article teaches several enzymes derived from a specific species of Candida which have distinct activities with regard to the reduction of specific chemicals (e.g., TABLE 2).

However, commensurate with Applicant's argument of 4/25/08 (pp. 12-13), it is clear that Wada also notes that several substrates will not work with specific enzymes, and there is simply no way to reasonably predict which of the enzymes, or which other enzymes will produce the activity required of reducing the pentanones and with the stereoselectivity required, in any specific embodiment.

Applicant's specification Broadly teaches many sources of enzyme and broadly states that these enzymes may be used to obtain the various isomers with the various stereoselectivity.

Applicant's examples teach specific encoded deposits of enzymes pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, without reference to which enzyme is which, and from where it is obtained. Hence, the Examiner cannot determine more from this than that the specific enzymes will work.

Still further, it is clear from the specification, that the enzyme source is self-determining (e.g., definiton of Enzyme Source, p. 14), without any more elaboration as to which enzyme sources actually have the activity.

Therefore, the Artisan would have to experiment to find those portions of the cells that would produce the required reduction and those that would so-reduce the compound even though disrupted, and determine which isomer would be produced (i.e., S or R), as well as determine those enzymes encompassed which produce the particular activity.

Such experimentation is considered undue as it is required to reasonably predict the breadth of Applicant's claimed invention for Applicant.

Response to Argument – Enablement

Applicant's argument of 4/7/09 has been fully considered but is not found persuasive.

Applicant argues that the claims are enabled for their breadth, as the enzymes are clarified, and claim 13 does not state the enzyme required (p. 10).

Such is not persuasive, for reasons provided above. The claims are poorly amended and specifically detach any enzyme listed from being required. Claim 13 is broader, encompassing the same compositions as Claim 1, as well as any organic chemistry method. Hence, it is also rejected on these bases.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633